

Original Article

Carbohydrate Overnutrition Harmfull to both Obese Pregnant Mice and Fetuses

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ABSTRACT

Background: Obesity in pregnancy due to carbohydrate overnutrition is still rarely reported, and the incidence of obesity in pregnancy in developing countries has begun to increase. This study aims to observe the detrimental effect of obesity in mothers and developing fetuses of mice fed a high carbohydrate diet. **Methods:** The obese group was fed a high carbohydrate (HC) diet, and the control group had a standard diet for 12 weeks. All mice were mated until they were pregnant and terminated for blood collection every trimester. Seven mice from the obese group and 7 mice from the control group were followed until 3rd trimester and then terminated for blood collection. Blood lipid profile and glucose were examined by photometrics, while anthropometric variables were measured by weight scale and meter scale. **Results:** Maternal obesity was associated with significantly elevated blood triglyceride levels in the first and second trimesters. At the same time, no significant differences were observed in blood glucose, total cholesterol, HDL, and LDL levels between the obesity and normal weight groups in the third trimester. Furthermore, fetuses of obese mothers exhibited significantly increased birth weight, length, head circumference, and waist circumference compared to those of normal-weight mothers. **Conclusion:** Obesity in pregnancy due to carbohydrate overnutrition could have detrimental effects on both the mother and developing fetuses.

1. INTRODUCTION

Obesity has become a significant problem worldwide, include obesity in pregnancy.^(1,2) Obesity in pregnancy have many detrimental effects for both mother and developing fetuses in the uterus, and the risk for future childhood. Hypertension in pregnancy, cesarean section delivery, macrosomia, and obesity in childhood are among the effects of obesity in pregnancy that have always been reported.^(3,4,5)

In developed countries, obesity commonly due to high-fat consumption and leads to metabolic diseases in both mothers and fetuses.^(6,7) Inversely, in developing countries, high carbohydrate consumption may cause obesity in pregnancy.^(8,9) and has a negative impact on both mother and fetus and maybe by different mechanisms. Excessive carbohydrates because of high glycemic index could interfere with the metabolic status of pregnant mothers.^(10,11)

It is believed that high levels of glucose and profile lipid alteration are the underlying mechanisms that lead to negative influence for both mothers and fetuses in high-fat diet.^(12,13,14) There are limited studies focused on carbohydrate nutrition on obesity in pregnancy and their impact on mothers and fetuses, and we hypothesized that obesity in pregnancy due to carbohydrate overnutrition alone could have a detrimental effect on both mothers and fetuses, as shown in high-fat diet as well.

The objective of this study is to observe the detrimental effect of obesity in both mother and developing fetuses of mice fed a high carbohydrate diet.

2. METHODS

Animal

Mus musculus females were maintained in the Animal Laboratory of the Medical Faculty of Hasanuddin University. All mice were maintained at 28-30°C temperature on a 12 h light and 12 dark cycles. Female mice, 8 weeks of age with a weight of 15-16 grams, were divided into two groups. Group 1 was fed a high carbohydrate (HC) diet, and Group 2 was the standard diet for 12 weeks. All mice in group 1 with a weight > 36 grams (obesity group) and in group 2 with a body weight < 25 grams (normal weight group) were recruited in this study. All groups mated until they were pregnant and terminated for collecting blood with cardiac puncture every trimester for examining blood glucose and triglyceride. Furthermore, 7 mice from the obese group and 7 mice from the control group were followed until 3rd trimester and then terminated to collect the blood lipid profile and examine the fetuses' anthropometry. In this study, the duration from the animal to be pregnant (fertilization) until delivery is about 21-23 days, and every trimester consists of 7 days. All protocols for this study were accepted by Hasanuddin University's Medical Faculty Ethical Board, with the registered number UH14070398.

Diet

The mice were fed by HC for the obese group and standard diet for the control group. The HC diet consists of carbohydrate 75%, fat 5%, protein 17%, and vitamin 1%, while the standard diet consists of carbohydrates 5%, fat 4%, protein 19%, calcium 0,5-1,1%, and phosphor 0,5-0,7 1%. The HC diet was produced by the Nutrition Department Animal Husbandry Faculty of Hasanuddin University, and the standard diet was bought from the animal diet market.

Laboratory assays

Lipid profiles such as triglycerides, LDL, and HDL were measured with enzymatic photometric technique (ABX Pentra 400) in Makassar District Health Laboratory. The colorimetric indicator is quinoneimine which is generated from 4-aminoantipyrine and phenol by hydrogen peroxide under the catalytic action of peroxidase (Trinder's reaction). Blood glucose is examined by a glucometer kit (Accu-check) with an enzyme on the Accu-check strip that converts the glucose in the blood sample to gluconolactone. Anthropometry status was determined by using a digital weight scale (Furi FEC 150) and a tailor-meter scale.

Statistical analysis

All data were normally distributed and were shown as mean \pm standard deviation of the mean. An independent sample t-test was used to compare body weight, blood glucose, and TG level every trimester, lipid profile, and anthropometric measurement in 3rd trimester between group 1 and group 2. Paired t-test was also used to compare the change of blood glucose and triglyceride every trimester in group 1 and group 2 mice.

3. RESULTS

Table 1. The animal's body weight in each trimester before terminated

	Obese group (gr)	Control group (gr)	p
	Mean \pm SD	Mean \pm SD	
Trimester 1	41,5 \pm 2,11	27,9 \pm 0,98	< 0.001
Trimester 2	51,4 \pm 0,97	37,3 \pm 3,27	< 0.001
Trimester 3	59,0 \pm 1,10	42,0 \pm 1,37	< 0.001

p : Independent sample *t* test

The data showed (Table 1) that the body weight before termination increased significantly ($p < 0,05$) in the obese group compared to the control group as well. The HC diet was successful in increasing the weight body of the experimental animal as expected.

Table 2. Blood glucose and triglyceride levels in the obese group and the control group during pregnancy

Variables	Obese group (n = 16)	Control group (n = 18)	p
Glucose (GDS) mg/dl	Mean ± SD	Mean ± SD	
Trimester 1	181.0 ± 48.51 ^a (5)	184.7 ± 29.24 ^c (6)	0.880
Trimester 2	172.2 ± 40.18 ^a (6)	217.3 ± 98.06 ^c (6)	0.321
Trimester 3	188.8 ± 61.42 ^a (5)	203.8 ± 56.63 ^c (6)	0.683
Triglyceride (TG) mg/dl			
Trimester 1	118.2 ± 22.03 ^b (5)	78.0 ± 17.47 ^d (6)	0.008*
Trimester 2	117.5 ± 32.92 ^b (6)	66.8 ± 18.90 ^d (6)	0.008*
Trimester 3	178.0 ± 79.67 ^b (6)	114.3 ± 62.12 ^d (6)	0.154

* Independent sample t test $p < 0.05$, n = number of mice

a,b,c,d superscript for Paired t test, $p > 0.05$ for same superscript

Table 2 showed an alteration of glucose and triglyceride serum levels every trimester in both groups. Triglyceride serum, particularly in 1st trimester and 2nd trimester, increased significantly (Independent sample t-test, $p = 0,008$) in the obesity group, but blood glucose levels did not change significantly in both groups. No significant difference (Paired t-test) for blood glucose and triglyceride changed every trimester.

Table 3. Third trimester of pregnancy of lipid profiles and fetuses anthropometric in the obese group and the control group

Variables	Obese group (n=7)	Control group (n=7)	p
Lipid Profile	Mean ± SD	Mean ± SD	
Cholesterol (mg/dl)	68.0 ± 21.49	84.4 ± 33.90	0.300
HDL (mg/dl)	36.9 ± 12.03	40.4 ± 16.23	0.648
LDL (mg/dl)	6.6 ± 1.13	11.7 ± 8.08	0.121
TG (mg/dl)	191.4 ± 89.3	164.4 ± 102.89	0.609
Fetuses anthropometric			
BW (gr)	1.4 ± 0.18	0.6 ± 0.08	< 0.001*
BL (mm)	2.4 ± 0.11	1.9 ± 0.15	< 0.001*
HC (mm)	3.0 ± 0.22	2.4 ± 0.11	< 0.001*
WC (mm)	2.8 ± 0.19	2.2 ± 0.07	< 0.001*
AC (mm)	0.9 ± 0.07	0.9 ± 0.05	0.109

* Independent sample t test

BW : bodyweight, BL : Bodylengths; HC : Head circumference; WC : Waist circumference; AC : Arm circumference

Lipid profile in 3rd trimester did not differ significantly. Still, anthropometric variables were substantially higher (Independent sample t-test, $p < 0,05$), except arm circumferences, in fetuses from the obesity group, as shown in Table 3.

4. DISCUSSIONS

Our data showed that carbohydrate overnutrition leads to obesity in mice, increases triglyceride (TG) serum, especially in the first and second trimesters, and increases the anthropometric size of fetuses. These data are in line with many studies reported before, although obesity in those studies due to high-fat nutrition or high-fat and high-carbohydrate nutrition.^(15,16,17,18)

Blood glucose did not differ between the obese and the control groups in every trimester, although we found a raised anthropometric size in the obese group. In diabetic pregnancy, blood glucose was believed to have a strong role in increasing the fetus size,^(19,20) but in obese person the data was still scarce. This study revealed that blood glucose was not associated with macrosomia in the fetuses. This data is in line with mice.⁽²¹⁾ However, in another study,⁽²²⁾ by using a fructose diet for mice, the blood glucose and body weight were increased compared to control mice.

In this study, we used a diet with carbohydrates (not fructose) and a lack of data about diets high in carbohydrates alone for mice, especially for pregnancy outcomes. To our knowledge, this is one of the very limited studies obtained to examine the detrimental effect of high carbohydrate nutrition alone on both mother and fetus size. The data showed that the detrimental effect also persisted in fetuses, as did the effect of a high-fat diet.

Blood lipid profiles such as cholesterol, HDL, LDL, and TG did not differ in 3rd trimester in the obese group compared to the control group (table 3), but TG tended to increase every trimester and was significantly higher in 1st trimester and 2nd trimester in the obesity group (table 2). The ascending of TG leads to an increase in the anthropometric size of fetuses in obese mice. TG also reported induced macrosomia (large of gestational age) and produced hypertension in gestational females.^(23,24) Furthermore, a higher level of TG in early gestational age was associated with gestational diabetes mellitus (GDM), which produced macrosomia and is also related to cardiovascular risk for mothers.^(25,26)

The increased level of TG, without being followed by blood glucose in our data, may be a special alteration in terms of a carbohydrate-over-nutrition diet – not in high fat or high fat and high carbohydrate diet – in mice models. These data could be preliminary data to provide a comprehensive study of obesity in pregnancy in poor people, which was caused by carbohydrate overnutrition. The increase in obesity in a poor country could be explained by this study that overnutrition of carbohydrates leads to obesity in the mothers and macrosomia of the fetuses.

5. CONCLUSION

It was concluded that obesity in pregnancy due to carbohydrate overnutrition could have detrimental effects on both mother and developing fetuses.

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Conflict of Interest Statement:

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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